



## Brief Report

# Low-dose ketamine analgesia: patient and physician experience in the ED<sup>☆</sup>

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### Abstract

**Objective:** Low-dose ketamine (LDK) may be useful for treatment for opioid-tolerant patients. We conducted a survey of patients and their treating clinicians regarding LDK for analgesia.

**Methods:** Survey data included the following: vital signs and pain score before and after LDK, demographics, and adverse effects. Treating physicians were queried about reasons for use of LDK and overall satisfaction.

**Results:** Twenty-four patients were enrolled: 21 received LDK for analgesia, and 3 received LDK for sedation. Pain level on a visual analog scale (range, 1–10) after LDK was significantly decreased from  $8.9 \pm 2.1$  to  $3.9 \pm 3.4$  ( $P < .0001$ ). Change in vital signs after administration of LDK was not statistically significant. Overall patient satisfaction with LDK was 55%, and overall physician satisfaction was 72%. Sixteen (67%) of patients would prefer LDK again, and 23 (96%) of physicians would use LDK again for analgesia. Four patients reported an adverse experience, but there were no emergence reactions. Race subanalysis revealed no difference in pain reduction, but whites were least satisfied compared with black and Hispanic patients ( $P = .02$ ). Physician reasons for using LDK included opioid failure (88%), concern for respiratory depression (17%), concern for multiple opioid allergies (13%), and concern for hypotension (8%). Most (96%) physicians believed that LDK is underused.

**Conclusion:** Low-dose ketamine may decrease patients' perception of pain. Most were satisfied with LDK for this purpose and would use it again. Whites were least satisfied with the use of LDK for analgesia. Physicians believed that ketamine is underused.

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## 1. Introduction

Ketamine (Ketalar) has been used extensively in the emergency department (ED) for conscious sedation and rapid sequence induction [1]. It has been more commonly used in pediatric than adult patients by emergency physicians. Ketamine, when used at lower subdissociative dosage (0.2

mg/kg IV), provides analgesia with less pronounced psychoactive side effects [2]. As such, ketamine may represent an alternative agent to opioids for patients with acute or chronic pain and may be advantageous for those who are opioid tolerant [3]. We conducted a survey study of ED patients receiving low-dose ketamine (LDK) specifically for analgesia to determine (1) level of pain reduction, (2) overall satisfaction with ketamine, (3) adverse side effects, and (4) willingness to be treated with ketamine again. We also surveyed their treating physicians regarding their satisfaction with LDK as an analgesic and potential reasons why ketamine is not commonly used for this indication in the ED.

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## 2. Methods

This was an observational case series performed during April 2011 at an urban university-based medical center ED serving a community of 1.5 million. It is a level 1 trauma center and also serves as a tertiary referral center to central and northern California. The ED has an annual volume of 70000 patient visits and an associated emergency medicine residency program. Patients were eligible for the study if they were aged 18 years or older and were to receive ketamine for any reason. Exclusion criteria included inability to understand English, cognitive impairment for whatever reason, or mental handicapped status. Their treating physicians were also enrolled in the study.

Patients about to receive ketamine were approached and asked if they would be willing to complete a survey regarding their experience. If they agreed, informed consent was obtained from the patient and their physician before administering the survey. Patient and physician data and responses were collected before and after administration of ketamine. Data included demographics, indications for using ketamine, vital signs before and after ketamine, adverse drug reactions, and any analgesics or sedatives administered before ketamine. The

survey instrument is shown in Figs. 1 and 2. Data were analyzed with STATA 12 (Stata Corp., College Station, TX), and statistical significance was assumed at a level of  $P \leq .05$ . This study was approved by our institutional review board.

## 3. Results

Over a 1-month period, 25 patients were identified, and 24 were enrolled. The average age for the study group was  $39.8 \pm 12.4$  years, with 16 women (64%) and 9 men (36%). With regard to race, there were 6 black (24%), 5 Hispanic (20%), 14 white (56%), but no Asian patients. Twenty-one patients received ketamine specifically for analgesia, and 3 received ketamine for sedation. One received ketamine for rapid sequence intubation and was not enrolled. The average dose of ketamine was  $22.2 \pm 11.2$  mg, and 2 repeat doses were given averaging  $12.5 \pm 3.5$  mg.

Vital signs before and 15 minutes after administration of ketamine were recorded. Average heart rate (beats per minute) before ketamine was  $84.4 \pm 19.4$  vs  $86.8 \pm 16$  after ( $P = .38$ ). Systolic blood pressure (millimeters of mercury) before was  $138.5 \pm 32.9$  vs  $146.8 \pm 30.2$  after ( $P = .06$ ).

**Ketamine Patient Survey**

MR# \_\_\_\_\_ Age \_\_\_\_\_ Gender \_\_\_\_\_ Race \_\_\_\_\_

Indication: Sedation \_\_\_\_\_ Analgesia \_\_\_\_\_ Chemical Restraint \_\_\_\_\_ RSI \_\_\_\_\_

Vital signs (use values recorded just before and right after Ketamine given):

HR before Ketamine _____	HR after Ketamine _____
SBP before Ketamine _____	SBP after Ketamine _____
RR before Ketamine _____	RR after Ketamine _____

Dosage of Ketamine \_\_\_\_\_ Route IV IM Repeat? Yes No

If used for analgesia:

Pain score (10 point scale) before Ketamine \_\_\_\_\_ Pain score after Ketamine \_\_\_\_\_

Adverse drug reaction? No Yes (if Yes, what?) \_\_\_\_\_

Analgesics/sedatives given prior to Ketamine \_\_\_\_\_

**Patient Questions:**

How satisfied were you with Ketamine? (have patient circle on line)  
 Not at all \_\_\_\_\_ Extremely

What was the best part of your experience with Ketamine?  
 \_\_\_\_\_

What was the worst part of your experience?  
 \_\_\_\_\_

Would you prefer to be given Ketamine again if needed at a future time? Yes No

**Fig. 1** The survey instrument: patient questions.

**Ketamine Clinician Survey**

How many years have you practiced Emergency Medicine\_\_\_\_\_?

If you chose Ketamine for analgesia, why? (circle all that apply)

Opioids not working  
 Concern for respiratory depression from opioids  
 Concern for hypotension from opioids  
 Multiple allergies to opioid analgesics  
 Other\_\_\_\_\_

How satisfied are you with Ketamine for analgesia in this case? Circle on line

Not at all\_\_\_\_\_Extremely

Would you use Ketamine again for analgesia?\_\_\_\_\_

Do you believe Ketamine is underutilized for analgesia in adult patients? Yes No

If yes, what are some reasons you believe may be the cause?

Emergence reaction  
 Hypertension  
 Laryngospasm  
 Better drugs available for indication  
 Restrictions on use  
 Limited literature on adult use compared to children  
 Other\_\_\_\_\_

**Fig. 2** The survey instrument: physician questions.

Respiratory rate (breaths per minute) was  $17.9 \pm 2.6$  before and  $17.6 \pm 4.2$  after ( $P = .5$ ). Change in heart rate, systolic blood pressure, and respiratory rate before and after administration of ketamine was not statistically significant from paired *t* test analysis.

Patients recorded their pain level on a 0 to 10 pain scale before and after administration of ketamine, and their pain level was significantly decreased from  $8.9 \pm 2.1$  to  $3.9 \pm 3.4$  ( $P < .0001$ , Wilcoxon test). Three patients reported no change in the pain level, 4 patients reported a change from 10 to 0, and no patient reported an increase in their pain level after receiving ketamine. Eighteen patients (75%) received 1 dose of opioid analgesics before ketamine with no improvement in their pain score after 30 minutes: 13 had hydromorphone, 3 had morphine, and 2 had fentanyl. Overall patient satisfaction with ketamine for analgesia was queried on a visual analog scale (range, 1-10 cm) and was  $55\% \pm 37.9\%$ ; physician satisfaction was  $71.7\% \pm 35.5\%$ . Sixteen (67%) of the patients would prefer to be given ketamine again, and 23 (96%) of physicians would use ketamine again for analgesia.

Sex subanalysis revealed that men reported an average decrease in pain level of  $5.0 \pm 3.9$ , and women reported  $4.9 \pm 3.8$ . This sex difference was not significant ( $P = .4$ , Mann-Whitney *U* test). Race subanalysis also revealed no significant differences in pain reduction, with black patients reporting an average decrease in pain of  $4.8 \pm 2.5$ ; Hispanics,

$7.2 \pm 3.3$ ; and whites,  $4.2 \pm 4.3$  ( $P = .35$ , analysis of variance). Whites were least satisfied with the use of ketamine ( $36.9 \pm 35.4$ ) when compared with black ( $70\% \pm 24.5\%$ ) and Hispanic ( $84\% \pm 35.4\%$ ) patients ( $P = .02$ , analysis of variance). Four patients reported an adverse experience, but there were no emergence reactions. Patient responses to the best and worst parts of their ketamine experience are summarized in Tables 1 and 2.

Physicians reported that average of years of practice was  $6.0 \pm 5.3$  with a range of 1 to 16 years. Physician reasons for using ketamine included opioid failure (88%), concern for respiratory depression (17%), concern for multiple opioid allergies (13%), and concern for hypotension (8%). Nearly all (96%) physicians believed that ketamine is underused for adult patients. Reasons for perceived underuse

**Table 1** Quotes: patients' best experiences with ketamine

"I have no pain now."  
 "I have decreased pain."  
 "I was floating then flying."  
 "I was in heaven."  
 "I was on a roller coaster."  
 "I was in a science fiction movie."  
 "I was on TV."  
 "I was a hippie."  
 "It was pure euphoria."

**Table 2** Quotes: patients' worst experiences with ketamine

"It was short-lived."  
 "It caught me off guard."  
 "I was out of my body."  
 "I had fuzzy vision."  
 "I couldn't speak."  
 "It was scary."  
 "I was floating."  
 "I was in quicksand."  
 "It was hard to focus."  
 "It made me sleepy."  
 "I was scared."  
 "I was hot."  
 "I was itchy."

are summarized in Table 3, with concern for emergence reaction being foremost (88%).

#### 4. Discussion

Patients with acute and chronic nonmalignant pain often have opioid tolerance from prolonged use of prescription and nonprescription opioid analgesics [3]. These patients may also have genetic polymorphism with resultant baseline resistance to opioid analgesia [4,5]. They may require multiple and higher than normal doses of opioids to achieve acceptable analgesia. High doses of opioid analgesics for these patients should be avoided whenever possible. Furthermore, parenteral opioid use in a subset of chronic pain patients may actually enhance pain sensitivity [6]. Alternative medications, such as ketamine, may be considered during these scenarios.

Chronic pain and opioid tolerance has been associated with up-regulation and activation of *N*-methyl-D-aspartate receptors within the central nervous system [3-5]. Ketamine is an *N*-methyl-D-aspartate receptor antagonist that has been shown to be an effective analgesic in many clinical studies. There is evidence that ketamine also inhibits morphine metabolism, thus increasing duration of analgesia, and that it has intrinsic anti-inflammatory effects [7,8]. Low-dose ketamine has been shown to mitigate pain and reduce opioid

**Table 3** Physician's reasons for ketamine underuse for adult patients

Potential emergence reaction (88%)  
 Concerns for restrictions on use (42%)  
 Limited literature on adult use compared to children (29%)  
 Can't use in patients with hypertension (17%)  
 Better drugs are available (17%)  
 Potential laryngospasm (8%)  
 Ignorance (4%)  
 Nursing concerns (4%)  
 Stigma (4%)

consumption in those with complex regional pain and postoperative patients who have undergone thoracoabdominal, maxillofacial, orthopedic, oncologic, obstetric, dental, and burn surgeries [9-19].

Most research on this topic has been published in the anesthesia and surgical literature. To date, there have been few ED studies involving ketamine for analgesia. Lester et al [20] evaluated 35 patients who received LDK for analgesia and reported that 19 (54%) experienced pain relief after opioid analgesics had failed. There were no adverse effects of ketamine in their study. Sih et al [21] reviewed several ED studies of the addition of ketamine to propofol ("ketofol") during conscious sedation in the ED and reported better analgesia and satisfaction for these patients than those receiving propofol alone. Low-dose ketamine has been used in the prehospital setting for treatment of pain associated with long-bone fractures; Johansson et al [22] found that addition of LDK significantly improved pain scores over those who just received morphine. Their results were similar to ours in that it was also associated with a rise in systolic blood pressure, although in our study, this did not reach statistical significance.

An unexpected finding of our study was the psychedelic effects of LDK reported by patients (Tables 1 and 2). Many patients reported these as negative experiences possibly because it was unexpected. Psychedelic hallucination associated with ketamine is thought to be a dose-dependent phenomenon, but based on our results, this side effect occurs with lower than normal dosage [23]. We believe that discussing these possible side effects of ketamine with the patient before administration may preclude negative experiences. From our extensive past use of ketamine for all indications (before this study) and in a wide dosage range, we have also found that describing these potential psychedelic effects as positive experiences before and during ketamine treatment greatly reduces negative outcome and emergence reaction. In our study, no patients experienced emergence reactions with LDK.

Most research on ketamine in the ED is from use in pediatric patients for conscious sedation. Reluctance to use ketamine for analgesia and in adult patients was recognized by the physician subjects of this study as well as a dedicated ketamine research group [1]. The 2 most common concerns cited were emergence reaction and hospital-specific restriction on ketamine use. In our findings, there were no emergence reactions with LDK, and the study was indeed halted because of restrictions placed on ketamine use soon after the study began. These restrictions on ketamine were imposed independent of our study. In the past, ketamine was restricted from use in the ED by anesthesiologists who believed that emergency physicians were unqualified to perform conscious sedation with ketamine; this has become less of an issue today [24]. It is extensively used by the military to treat pain from combat injury [25]. Ketamine had been successfully used for analgesia by prehospital providers in Europe and Australia [26]. Low-dose ketamine has been

successfully used to treat adult depression and suicidal ideation [27]. We believe that as emergency physicians become more informed about the safety of LDK, it may be accepted as an alternative to repeated high doses of opioid analgesics in otherwise tolerant patients.

## 5. Limitations

This study has several limitations. First, it is a small sample of patients with limited power. It is a survey study with subjective answers regarding pain perception and satisfaction and subject to variability. Patients' perception of pain may differ widely from a pharmacogenetic and temporal standpoint, and this could have affected our results. Even if this study were randomized and double blinded, patients' report of pain would still be subjective. We do believe, however, that this is the next step in the evaluation of LDK for analgesia in the ED.

## 6. Conclusion

Low-dose ketamine as an adjuvant to opioids may decrease patients' perception of pain. Most patients and physicians were satisfied with ketamine for this purpose and would use it again. Whites were least satisfied with the use of ketamine for analgesia. Physicians believed that ketamine is generally underused in adult patients.

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